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10/591,612	07/16/2007	Teruo Okano	GRT/159-102	3397

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EXAMINER	
WILSON, MICHAEL C	
ART UNIT	PAPER NUMBER
1632	
MAIL DATE	DELIVERY MODE
09/28/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,612	OKANO ET AL.	
	Examiner	Art Unit	
	MICHAEL WILSON	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 September 2011*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *22,25-36 and 40-43* is/are pending in the application.

5a) Of the above claim(s) *25 and 40* is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *22,26-36 and 41-43* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9-9-11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9-9-11 has been entered.

Claims 1-21, 23, 24, 37-39 have been canceled. Claims 42, 43 have been added. Claims 22, 25-36, 40-43 are pending.

Election/Restrictions

Claims 25 and 40 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicants request rejoinder without providing any arguments. The claims remain withdrawn because the mouse or rat does not have to be made using the method of claims 22 or 27.

Claims 22, 26-36 and 41-43 are under consideration.

Applicant's arguments filed 9-9-11 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Applicants are reminded that they must provide support for each new phrase and claim in an amendment. Support for each new phrase and claim should be provided in the opening paragraphs of each response by applicant. Failure to do so may result in a new matter rejection if support is not readily apparent. Applicants should provide support for each phrase and claim using page and line numbers of the specification as originally filed. Do not simply use paragraph numbers.

Claim Rejections - 35 USC § 112

New Matter

The rejection of claim 22 regarding "but the cell culture support is not a mixture of a polymer and collagen" has been withdrawn because the phrase has been deleted.

The rejection of claim 22 regarding the phrase "without being treated with a proteolytic enzyme or ethylene glycol bis)2-aminoethylether) tetraacetic acid (EGTA)" has been withdrawn because the phrase has been deleted.

The rejection of claim 27 regarding the phrase "the hydration force of which changes in a temperature range of..." has been withdrawn because the phrase has been deleted.

The phrase "nude rat" in claims 22 and 27 is new matter. Pg 12, paragraph 24, supports nude mice, rats, and mice, but does not explicitly or implicitly support nude rats as claimed.

The rejection of claim 27 regarding the phrase "at a temperature at which the polymer has a weak hydration force" has been withdrawn in view of pg 3, paragraph 7, line 6-7.

The rejection of claim 27 regarding the phrase "on which transplantation is to be performed" has been withdrawn in view of the abstract which was filed 7-16-07 as part of the original disclosure.

The rejection of claim 28 has been withdrawn in view of original claim 2.

The rejection of claim 29 has been withdrawn in view of original claim 3.

The rejection of claim 30 has been withdrawn in view of original claim 5.

The rejection of claim 31 has been withdrawn in view of original claim 6.

The rejection of claim 32 has been withdrawn in view of pg 6, paragraph 14.

The rejection of claim 33 has been withdrawn in view of original claim 7.

The rejection of claim 34 has been withdrawn in view of original claim 8.

The rejection of claim 35 has been withdrawn in view of original claim 9.

The rejection of claim 36 has been withdrawn in view of original claim 10.

The rejection of claim 41 has been withdrawn in view of claim 16 in the preliminary amendment filed 7-16-07 which is considered part of the original disclosure.

Claims 22, 26-36 and 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The concept of a "homo- and/or co-polymer" in claims 22 and 27 is new matter. Pg 7, paragraph 16, supports homo- or co-polymers and pg 11, line 1, supports poly(N-

isopropylacrylamide); however, the concept of a "homo- and/or co-polymer" cannot be found in the specification originally filed.

The concept of "culturing the human cancer cells on the celll [sic] culture support at a temperature at which the polymer has a strong hydration force" in claim 27 remains new matter. Applicants point to pg 3, paragraphs 7 and 8; however, the paragraph 7 merely states the culture solution was adjusted to a temperature at which the polymer had a stronger hydration force which is a different scope than a "strong" hydration force as now claimed.

Enablement

The rejection regarding using any polymer obtained by homo- or co-polymerization of one or more monomers that would detach in a sheet without being treated with a proteolytic enzyme or EGTA as broadly claimed other than poly(N-isopropylacrylamide) has been withdrawn because the claims have been limited to using poly(N-isopropylacrylamide).

The rejection of claim 26 (and claim 41 which should have been included) regarding selecting agents that treat tumors by administering a test substance to a nude mouse or nude rat before and/or after transplanting human cancer cells has been withdrawn in view of pg 16, Example 3, and the art at the time of filing.

Claims 22, 26-36 and 41-43 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making a non-human animal having transplanted cancer cells comprising i) preparing a cell culture support coated with poly

N-isopropylacrylamide, ii) cultivating cancer cells on the cell culture support at a temperature in which the cells adhere and grow, iii) decreasing the temperature so that the cancer cells detach from the support, and iv) transplanting the detached cancer cells to a non-human animal, does not reasonably provide enablement for any polymer that changes its hydration force as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claim 22 is drawn to a process for preparing a cancer cell-transplanted non-human animal comprising:

(a) preparing a cell culture support coated on a surface, wherein the cell culture support is comprised of a polymer which shifts from a dehydrated state to a hydrated state in the temperature range of 0-80℃ but the cell culture support is not a mixture of a polymer and collagen, wherein the polymer is obtained by polymerization of one or more monomers selected from the group consisting of (meth)acrylamide compounds, N-(or N,N-di)alkyl-substituted (meth)acrylamide derivatives, and vinyl ether derivatives;

(b) cultivating cancer cells on the cell culture support at a temperature at which the polymer is dehydrated;

(c) cooling the cell culture support to a temperature at which the polymer is hydrated, whereby a sheet of cancer cells is detached from the cell culture support without being treated with a proteolytic enzyme or ethylene glycol bis(2-aminoethylether) tetraacetic acid (EGTA); and

(d) transplanting the sheet of cancer cells to a specified site of a non-human animal.

Claim 27 is drawn to a process for preparing a cancer cell-transplanted non-human animal comprising the steps of preparing a cell culture support coated on a surface with a polymer the hydration force of which changes in a temperature range of 0-80 ℃, wherein the cell culture support is not a mixture of a polymer and collagen, then cultivating cancer cells on the support in a temperature region where the polymer has weak hydration force, thereafter adjusting the culture solution to a temperature at which the polymer has a stronger hydration force, whereby the cultured cancer cells are detached from the cell culture support without being treated with a proteolytic enzyme or ethylene glycol bis(2-aminoethylether) tetraacetic acid (EGTA), and transplanting the detached cancer cells to a specified site of a non-human animal on which transplantation is to be performed.

The specification states JP 05/192138 taught a method of

> "skin cells cultivation comprising the steps of preparing a cell culture support which has a surface of its base coated with a polymer having an upper or lower critical temperature for dissolution in water in a range of 0-80℃, cultivating skin cells on the cell culture support at a temperature not higher than the upper critical temperature for dissolution or at a temperature not lower than the lower critical temperature for dissolution, and thereafter adjusting the temperature to above the upper critical temperature for dissolution or below the lower critical temperature for dissolution, whereby the cultured skin cells are detached. This method depends on temperature adjustment for detaching the cells from the culture base coated with the temperature-responsive polymer."

Example 1 describes a:

> "cell culture base was coated with the temperature- responsive polymer poly(N-isopropylacrylamide) in an amount of 2.0 μg/cm2 and the cancer cells

> NCI-H460 was cultivated (2 x 104 cells were seeded; 37℃ in 5% C02). Three days later, the cancer cells (NCI-H460) on the culture base were confirmed to have become confluent; thereafter, a cultured cell moving jig comprising a polyacrylic plate coated with a fibrin gel was gently placed over the cultured cell sheet so that the cultured cancer cells adhered to it; then, the cell culture base was cooled at 20℃ for 60 minutes. After the cooling, the detached cell sheet was collected from the jig together with the fibrin gel and a piece of the gel with the adhering cell sheet (7 mm x 17 mm x 2 mm; 5 x 10^5 cells) was transplanted subcutaneously to the back of each of 10 nude mice" (pg 13).

Paragraph 16, pg 7-8, teaches the polymer can be obtained by homo- or copolymerization of monomers selected from the group consisting of monomers include (meth)acrylamide compounds, N- (or N,N- di)alkyl-substituted (meth)acrylamide derivatives, and vinyl ether derivatives.

Rejections

Claims 22 and 27 are not enabled for performing the method in a nude rat. The claims encompass transplanting human cancer cells into any nude mouse or nude rat, and the specification suggests making a nude mouse, rat, mouse, guinea pig, and rabbit and exemplifies making a nude mouse. The specification states the cancer cells can be from humans (pg 6, paragraph 14, line 10-12). For the animal to support the growth of human cancer cells, it must not reject the cells. The only means described for maintaining human cancer cells in an animal model is if the animal is immunocompromised, and the only immunocompromised animal described by applicants is a nude mouse. If the animal is not immunocompromised, the cancer cells will be attacked by the host's immune system, be destroyed and fail to create a tumor. The specification does not teach or suggest using a nude rat and such an embodiment is not implicit from the teachings on pg 12, paragraph 24, which lists nude mouse,

mouse and rat separately. Overall, applicants fail to provide adequate guidance to use a nude rat with human cancer cells as claimed. Therefore, the claims should be limited to using a nude mouse.

Indefiniteness

Claims 22, 26-36 and 41-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The temperature "at which the polymer has weak hydration force" in claim 27 is indefinite. The metes and bounds of when a hydration force is "weak" are not defined in the specification or art at the time of filing. The specification does not teach how to determine when a polymer is in a temperature range that causes a weak hydration force. Without such guidance, those of skill would not be able to determine when they were infringing on the claim.

Applicants argue pg 3-4, paragraphs 7-8, discussed weak hydration forces and that a change from a weak to a stronger hydration force was required to release the human cancer cells from the cell culture support. Applicants' argument is not persuasive. The metes and bounds of what applicants consider a weak hydration force is the issue at hand, and the specification and the art at the time of filing do not provide such a definition.

Likewise, the temperature "at which the polymer has a strong hydration force" in claim 27 is indefinite. The metes and bounds of when a hydration force is "strong" are

not defined in the specification or art at the time of filing. The specification does not teach how to determine when a polymer is in a temperature range that causes a strong hydration force. Without such guidance, those of skill would not be able to determine when they were infringing on the claim.

Applicants argue pg 3-4, paragraphs 7-8, discussed strong hydration forces and that a change from a weak to a stronger hydration force was required to release the human cancer cells from the cell culture support. Applicants' argument is not persuasive. The metes and bounds of what applicants consider a strong hydration force is the issue at hand, and the specification and the art at the time of filing do not provide such a definition.

Claim 29 remains indefinite as amended because "a human cancer cell sheet to be transplanted is prepared in a specified shape of a specified size so that the size and/or shape of cancer tissue in the nude mouse or nude rat is controlled" does not make sense. It remains unclear what applicants are attempting to limit about the size and shape of the detached cancer cells sheet. Accordingly, it cannot be determined how the phrase further limits claim 27. Claim 29 can be written more clearly by indicating an active step of shaping or preparing the detached cancer cells, i.e. further comprising preparing the detached human cancer cells in sheet form into a specific shape.

Claim 31 is indefinite because the metes and bounds of when a cancer cell is from a "transplantable" cell line. Accordingly, the claim does not further limit the structure or function of the cell line. Applicants point to paragraph 14, bridging pg 5-6,

which discuss transplantable and untransplantable cells. Applicants' arguments are not persuasive. All cells are transplantable; therefore, claim 31 does not further limit claim 27. Whether or not they survive is irrelevant to whether they can be transplanted. In this case, the discussion on pg 5-6 fails to adequately define which cells are transplantable or describe structural or functional features of "transplantable" cells. When they are no longer considered "transplantable" cannot be determined; therefore, those of skill could not determine when they were infringing on the claim.

Claim 33 is indefinite because the metes and bounds of when a cancer cell is from an "untransplantable" cell line. Accordingly, the claim does not further limit the structure or function of the cell line. Applicants point to paragraph 14, bridging pg 5-6, which discuss transplantable and untransplantable cells. Applicants' arguments are not persuasive. All cells are transplantable; therefore, it cannot be determined how claim 33 further limits claim 27. Whether or not transplanted cells survive is irrelevant to whether they can be transplanted. In this case, the discussion on pg 5-6 fails to adequately define which cells are "untransplantable" or describe structural or functional features of "untransplantable" cells. When they are considered "untransplantable" cannot be determined; therefore, those of skill could not determine when they were infringing on the claim.

The metes and bounds of claim 35 are indefinite because all living cells are collected from living tissue. Applicants argue the claim is intended to distinguish the cells from living tissue from cell lines. Applicants' argument is not persuasive. Cell lines are "from living tissue" as claimed.

The rejection of claim 38 has been withdrawn because the claim has been canceled.

Claim 41 is indefinite because it never clearly set forth administering an agent to the nude mouse or nude rat made by the process of claim 27. Instead the claim as amended now requires "administering a test substance to a nude mouse or nude rat before and/or after transplanting human cancer cells therein during preparation of a human cancer cell-transplanted nude mouse or nude rat by the process according to claim 27", which does not make sense. The claim does not clearly set forth the substance is administered somewhere before, during or after the method steps of claim 27. In addition, claim 41 does not clearly indicate the substance is administered to the nude mouse or nude rat of claim 27 before and/or after the transplanting step (iv).

Claim Rejections - 35 USC § 102

Claims 27-31, 33, 35 remain and 42 and 43 are rejected under 35 U.S.C. 102(b) as being anticipated by Koezuka (Nippon Nogei Kagaku Kaishi, 1994, Vol. 68, No. 4, pg 783-792, abstract only) in view of applicants' arguments.

This rejection assumes Koezuka taught a poly(N-isopropylacrylamide) polymer as argued by applicants in the response filed 6-26-09, pg 12, and the conditions required to detach cells in a sheet as claimed.

Koezuka taught culturing human cancer cells from a primary culture on a thermoresponsive poly(N-isopropylacrylamide) polymer, detaching the cells from the polymer without trypsin and transplanting the cells to nude mice. The conditions

described by Koezuka inherently detach cells in a sheet as claimed because the cells are on poly N-isopropylacrylamide polymer and because the conditions are described by applicants as being part of the invention. The claims do not exclude using dextran sulfate or EGTA. Claims 31 and 33 are included because the primary culture described by Koezuka is either a transplantable or untransplantable cell line.

Response to arguments

Applicants' arguments state the invention of Koezuka is not used in the manner required by the claims. Applicants' argument is not persuasive because it fails to point to one specific step claimed that is not taught by Koezuka.

Applicants argue the substrate used by Koezuka is not the substrate used by applicants. Applicants' argument is not persuasive because it meets the limitations claimed.

Applicants argue Koezuka did not change the hydration force by changing the temperature. Applicants' argument is not persuasive. The claims do not require changing the temperature. The claims merely require changing the hydration force from "weak" to "strong" which can be performed at the same temperature. The change in hydration force claimed occurs in Koezuka as evidenced by the cancer cells detaching. Furthermore, the method described by Koezuka is described by applicants as being part of the invention.

Applicants argue the cell culture support claimed never changes to a liquid phase. Applicants' argument is unfounded. No such limitation is claimed. The claims use open language and encompass using collagen, dextran sulfate and EGTA

treatment. Furthermore, it is not readily apparent from the specification that applicants contemplated excluding collagen, dextran sulfate or EGTA. Specifically, pg 12, line 2, contemplates using collagen.

Claim Rejections - 35 USC § 103

The rejection of claims 22, 27-31, 33, 35 under 35 U.S.C. 103(a) as being unpatentable over Koezuka (Nippon Nogei Kagaku Kaishi, 1994, Vol. 68, No. 4, pg 783-792, abstract only) in view of Sakai (JP 05/192138) and Hirose (Biomacromolecules, 2000, Vol. 1, pg 377-381) has been withdrawn. Although the rejection still applies, the rejection was written to address the limitation "not a mixture of a polymer and collagen" in claims 22 and 27 which has been deleted in the claims as amended.

Claims 22, 27-31, 33, 35 remain and claims 42 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koezuka (Nippon Nogei Kagaku Kaishi, 1994, Vol. 68, No. 4, pg 783-792, abstract only) in view of Sakai (JP 05/192138).

Koezuka taught culturing human cancer cells from a primary culture on a thermoresponsive N-isopropylacrylamide polymer, detaching the cells from the polymer without trypsin and transplanting the cells to nude mice (see anticipation rejection above). This rejection assumes Koezuka did not teach the specific conditions required to detach cells using poly(N-isopropylacrylamide) polymer as in claims 22 and 27. In particular, the abstract of Koezuka did not teach "cooling the cell culture support to a temperature" in claim 22, step c) or without a proteolytic enzyme (e.g. EGTA) as in claims 42 and 43.

However, methods of culturing cells with poly (N-isopropylacrylamide) were known in the art as described by Sakai. The specification acknowledges that JP 05/192138 taught a method of

> "skin cells cultivation comprising the steps of preparing a cell culture support which has a surface of its base coated with a polymer having an upper or lower critical temperature for dissolution in water in a range of 0-80℃, cultivating skin cells on the cell culture support at a temperature not higher than the upper critical temperature for dissolution or at a temperature not lower than the lower critical temperature for dissolution, and thereafter adjusting the temperature to above the upper critical temperature for dissolution or below the lower critical temperature for dissolution, whereby the cultured skin cells are detached. This method depends on temperature adjustment for detaching the cells from the culture base coated with the temperature-responsive polymer."

Thus, the specific conditions required to detach cells in a sheet using poly(N-isopropylacrylamide) were known as supported by Sakai.

Thus, it would have been obvious to those of ordinary skill in the art at the time the invention was made to culture cancer cells on poly(N-isopropylacrylamide), detach the cancer cells from the primary culture using EGTA, and transplant the cells into nude mice as taught by Koezuka using the conditions for detaching cells from poly(N-isopropylacrylamide) in a sheet described by Sakai. Those of ordinary skill in the art would have been motivated to use the conditions for detaching cells in a sheet described by Sakai for ease of manipulation and to prevent leakage of the cells from the site of transplantation. Since the cells are attached to each other in a sheet, they would be less likely to leak from the site of transplantation.

The translation of Sakai shows Sakai taught performing the method in the absence of collagen and without EGTA (see Examples in Sakai) as in claim 22. Thus, it would have been obvious to those of ordinary skill in the art at the time the invention

was made to culture cancer cells on poly(N-isopropylacrylamide), detach the cancer cells from the primary culture, and transplant the cells into nude mice as taught by Koezuka in the absence of collagen or without EGTA as described by Sakai. Those of ordinary skill in the art would have been motivated to remove collagen to save money and time. Those of ordinary skill in the art would have been motivated to replace EGTA with any other compound known in the art at the time of filing that would detach cells in a sheet as the compounds were interchangeable. It was well within the purview of those of ordinary skill to choose any of a number of compounds capable of detaching cells in a sheet at the time of filing.

Those of ordinary skill in the art at the time of filing would have had a reasonable expectation of performing the method of detachment of skin cells using N-isoporpylacrylamide by decreasing the temperature as described by Sakai using cancer cells described by Koezuka because skin and cancer cells overlap (cancer cells can be skin cells) and because skin and cancer cells share significant culture similarities and because skin cells and cancer cells can be cultured under similar conditions.

Overall, the method of Koezuka transplanted a detached sheet of human cancer cells made (using N-isopropylacrylamide as acknowledged by applicants in the response filed 6-26-09, pg 12) onto a nude mouse, and Sakai merely taught the conditions required to detach the cancer cells from poly(N-isopropylacrylamide) by decreasing the temperature. If applicants believe the conditions required to detach cancer cells from poly(N-isopropylacrylamide) are different than those of Sakai, i.e. changing the temperature ("This method depends on temperature adjustment for

detaching the cells from the culture base coated with the temperature-responsive polymer"), clarification is required.

Response to arguments

Applicants summarize Koezuka and Sakai and argue Koezuka did not change the hydration force by changing the temperature. Applicants' argument is not persuasive. Only claim 22 requires cooling, and Sakai taught the cooling conditions required to detach cells using N-isopropylacrylamide.

Applicants argue the method of Sakai is limited to skin cells and not cancer cells. Applicants' argument is not persuasive. The claims encompass skin cells that are cancer cells. Furthermore, those of ordinary skill in the art at the time of filing would have had a reasonable expectation of performing the method of detachment of skin cells using N-isopropylacrylamide by decreasing the temperature as described by Sakai using cancer cells described by Koezuka because skin and cancer cells overlap (cancer cells can be skin cells) and because skin and cancer cells share significant similarities in culture and because skin cells and cancer cells can be cultured under similar conditions.

Applicants argue the documents teach away from applicants' invention and show lack of a reasonable expectation of success. Applicants' argument is not persuasive. It is unclear why applicants believe the references teach away from the claimed invention (or any specific embodiment described by applicants but not claimed). Those of ordinary skill in the art at the time of filing would have had a reasonable expectation of performing the method of detachment of skin cells using N-isopropylacrylamide by

decreasing the temperature as described by Sakai using cancer cells described by Koezuka because skin and cancer cells overlap (cancer cells can be skin cells) and because skin and cancer cells share significant similarities in culture and because skin cells and cancer cells can be cultured under similar conditions.

Applicants' argument regarding "poor take" and "efficacy is difficult" on pg 12, lines 1-4, of the response filed 9-9-11 is noted. Applicants' argument is not fully realized; however, a showing of difficulty or low efficiency is still considered successful and is all that is required to meet the limitations claimed.

Applicants' discussions of the "invention", of known cancer cell-transplanted animals, and problems with known cancer cell-transplanted animals on pg 12-13 of the response filed 9-9-11 are noted. Applicants' discussions do not constitute an argument. Those of ordinary skill in the art at the time of filing would have had a reasonable expectation of performing the method of detachment of cells using N-isopropylacrylamide by decreasing the temperature as described by Sakai using cancer cells described by Koezuka because skin and cancer cells overlap (cancer cells can be skin cells) and because skin and cancer cells share significant similarities in culture and because skin cells and cancer cells can be cultured under similar conditions. If applicants are attempting to argue the combined references are not enabled, clarification is required. It is noted, however, that it is completely within reason to believe that Koezuka decreased temperature as described by Sakai to detach the cancer cells. It is also within reason for those of ordinary skill in the art at the time of filing to expect that skin cells and cancer cells, specifically cancerous skin cells, would

behave similarly under the conditions described by Sakai because they share similarities in culture and can be cultured under similar conditions.

Applicants' arguments regarding improving known cancer-cell animal models are noted but are irrelevant. The claims are not "improvement" claims. Furthermore, the method of Koezuka produced an animal having such an improvement, and Sakai merely taught the conditions required to detach cancer cells from poly(N-isopropylacrylamide) by decreasing the temperature. If applicants believe the conditions required to detach cancer cells from poly(N-isopropylacrylamide) are different than those of Sakai, i.e. changing the temperature ("This method depends on temperature adjustment for detaching the cells from the culture base coated with the temperature-responsive polymer"), clarification is required.

Double Patenting

Claim 42 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 43. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday through Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Primary Patent Examiner